

### **Remarks**

Claims 1-7, 9-25 and 27-54 are pending in the application. Claims 34-36 and 40 stand rejected. Claims 7 and 48-54 are objected to. Claims 3, 6, 7, 9, 10, 13-15, 17, 18, 24, 27, 28, 35, 36, 38-40, and 43 are amended by the herein amendment. Reconsideration is respectfully requested in view of the following comments.

#### **I. Claim Amendment Summary**

Claims 3, 6, 10, 13, 15, 35, 36, 38, 39 and 43 are amended to clarify that each of the specifically recited heteroaryl rings may be either substituted or unsubstituted. This amendment is supported by the patent specification at column 3, line 41-42 in view of the definition of "aryl" disclosed at column 3, line 58-59 as including heteroaryl.

Claims 13 and 36 are also amended to remove "hydrogen" from the definition of X. The amended Markush group is supported by claims 13 and 36 as originally drafted because the original Markush group defining X provides support for the amended Markush group from which one element has been removed.

Claim 7 is amended herein to expressly recite the feature "phenyl, mono-substituted with hydroxyl, nitro, carboxy, C<sub>1</sub>-C<sub>6</sub> trihaloalkyl or cyano," as recited in claim 6 from which claim 7 depends. As amended, claim 7 further limits the subject matter of claim 6.

Claims 9, 14, and 24 are amended herein for clarity by inserting punctuation. In claims 9 and 14, a colon is inserted after the expression "wherein Z is the group." In claim 24 and 27, a colon was inserted after "a compound of formula I" and after "a compound of formula IV."

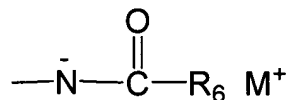
Claim 27 is amended to insert the missing article "a" in the expression, "with 4-sulfamyl phenyl hydrazine or a salt thereof." Claim 27 is also amended to delete the repeated word "wherein" after the structure of formula II. This amendment is supported by claim 27 in the issued patent, which does not repeat the word, "wherein."

Claim 28 is amended to delete the repeated word "wherein" after the structure of formula II.

Claim 40 is amended to recite that neoplasias treated by the method of the invention are those neoplasias that express a cyclooxygenase. Support for this feature in

the patent specification at column 12, lines 26-55 and in US patent 5,972,986, which is incorporated by reference into the '519 patent, at column 2, line 42-44.

Claims 17 and 18 are amended to clarify that the structure of the anion of the acylsulfonamide R<sup>5</sup> moiety:



does not have a proton on the nitrogen atom. The correction to the above structure is supported by the structure as shown in the Applicants' patent specification at column 6, line 35-40, wherein the anion structure does not have a proton on the nitrogen atom.

The structural change made in amending claims 17 and 18 was also made to new claims 53 and 54 which were introduced in the preliminary amendment, but which were objected to as being in improper format. Applicants attorney spoke with the Examiner by phone on June 16 to inquire whether the improperly formatted claims should be designated as "New" and completely underlined as directed in the present office action even if a change is made to the claim. The Examiner stated that the Preliminary Amendment filed with the present reissue application on July 29, 2003 had not been entered with respect to claims 48-54 because of the improper format of these new claims. The Examiner stated that a claim amendment in response to the April 15 Office Action should resubmit claims 48-54, with the entire text underlined as directed in the Action. The Examiner instructed Applicant's attorney to designate these claims as "new" even if the text is changed from that submitted in the July 29, 2003 Preliminary Amendment.

#### **Response to Objection to Claim 7 for Improper Dependency**

The Examiner objected to claim 7 as improperly dependent for failing to further limit the subject matter of claim 6. Claim 7 has been amended herein to positively recite the list of substituents on mono-substituted phenyl Z.

#### **Response to Objection to Claims 48-54 for Improper Format**

The Examiner has objected to new claims 48 to 54 as being in improper format for failure to underline the entirety of the new claims. As discussed briefly above, Applicants' attorney contacted the Examiner by phone to confirm that the correct

response to this objection was resubmission of claims 48-54 as “New” claims wherein the text is underlined in its entirety.

**Response to Rejection under 35 U.S.C. § 112, first paragraph**

Claims 34-36 and 40 stand rejected pursuant to 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Applicants respectfully submit that claims 34-36 and 40, including the herein amendment of claims 35, 36 and 40, are enabled under 35 U.S.C. § 112 1<sup>st</sup> paragraph.

Applicants enjoy a presumption that the specification, which discloses how to make and use the claimed invention, complies with the first paragraph of 35 U.S.C. 112, unless there is a reason to doubt the objective truth of the specification. See, *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). The initial burden of establishing a basis for denying patentability to a claimed invention rests upon the examiner. See, *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Thorpe*, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985); *In re Piasecki*, 745 F.2d 1468, 223 USPQ 785 (Fed. Cir. 1984).

The test of enablement is not whether *any* experimentation is necessary, but whether, if experimentation is necessary, it is undue. MPEP §2164.01 (citing *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976)). The fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. *Id.* Further, the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. MPEP §2164.05(a) (citing *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991)).

The Examiner alleges that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art. . . to make and/or use the invention.” The Examiner provides an analysis of some of the *Wands* factors (*In re Wands*, 8 USPQ2d 1400). The *Wands* factors analyzed by the Examiner are reviewed below.

A. The nature of the invention/Breadth of the claims

The Examiner correctly states that the invention is directed to a method of treating cyclooxygenase-mediated disorders (claims 34-36) and neoplasias (claim 40). The scope of claims 34-36 is commensurate with the disclosure because the claimed method of treating cyclooxygenase-mediated disorders comprises administering a compound selected from a defined genus shown to inhibit COX-2. The scope of claim 40, as herein amended, is also commensurate with the disclosure because the claim is directed to treatment of tumors that express cyclooxygenase, comprising administration of the disclosed COX-2 inhibitor.

B. State of the Art

The Examiner states that the state of the art “involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities, *i.e.* what compounds can treat which diseases and by what mechanism. (emphasis added)

As one threshold issue, Applicants believe that if “screening *in vivo* and *in vitro*” embodies the state of the art, then such experimentation would appear to be routine and therefore not undue experimentation. As a second threshold issue, Applicants point out that a necessary element of the claimed method of treatment is the mechanism of action, *i.e.*, cyclooxygenase-mediation. Thus, the practice of the invention does not require determination of the mechanism whereby the compounds act.

The Examiner’s analysis of the state of the art at the time of the Application neglects to mention the considerable amount of literature disclosing therapeutic potential of cyclooxygenase inhibitors, particularly COX-2 inhibitors, in treating tumors that express cyclooxygenase. See, for example, Gupta *et al.* (PMID:10579801, abstracting *Prostate*; 2000, 41(1); page 73-78) which states, “Aberrant or increased expression of cyclooxygenase (COX)-2 has been implicated in the pathogenesis of many diseases including carcinogenesis. COX-2 has been shown to be over-expressed in some human cancers.” Gupta’s analysis of data for COX-2 expression in prostate tissue showed utility of COX-2 inhibitors “for prevention or therapy of prostate cancer in humans.” See also, Yip-Schneider *et al.* (PMID:10657949 abstracting *Carcinogenesis*, 2000, 21(12), page 139-46) which states, “COX-2 expression is up-regulated in several types of human

cancers and has been directly linked to carcinogenesis.” Yip-Schneider evaluated the role of COX-2 in pancreatic cancer and concluded that “COX-2 may play an important role in pancreatic tumorigenesis and therefore be a promising chemotherapeutic target for the treatment of pancreatic cancer.” See also Ochaia *et al.* (PMID: 10665651, abstracting *Jpn. J. Cancer Res.*, 1999, 90(12), page 1338-43). Based on known COX-2 expression in various human cancers, Ochaia investigated COX-2 expression in non-small cell lung cancers (NSCLC) and concluded that “COX-2 may be associated with carcinogenesis of NSCLC, and that it may be a target for the treatment of NSCLC.” See also Komhoff *et al.* (PMID 10880372, abstracting *Am. J. Pathol.*, 2000, 157(1), page 29-35). Komhoff states that, “Studies in human and animal models have shown that COX-2 is up-regulated in several epithelial carcinomas including colon, breast, and lung.” Komhoff investigated COX-2 involvement in human bladder cancer and demonstrated “elevated expression of COX-2 in a high percentage of high-grade bladder carcinomas, suggesting a possible role of COX-2 in the progression of bladder urothelial carcinoma and supporting its potential as a therapeutic target in human bladder carcinoma.”

The references above (PubMed Abstracts attached hereto as Exhibit A) demonstrate that the state of the art includes recognition that tumors expressing a cyclooxygenase respond to treatment with a COX-2 inhibitor. The references further show that determination of cancers that express COX-2 constituted experimentation that did not rise above a level that was routine in the art.

#### C. Predictability in the Art

The Examiner states at page 5, lines 17-21 of the Action, that the pharmaceutical art is unpredictable, and that “each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.”

The Examiner’s language at page 5, line 17-21 in providing an alleged basis for undue experimentation mirrors the Examiner’s language at page 3, line 19-21 for the state of the art, *i.e.*, the state of the art . . . involves screening *in vitro* and *in vivo*. . .” Such apparent equivalency between experimentation that characterizes the state of the art and

experimentation required to practice Applicants' invention is inconsistent with an allegation that practice of the invention would require undue experimentation.

The Examiner, at page 4, line 15, cites Golub *et al.* "Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring" as evidence of unpredictability in the art of cancer therapy. The Examiner states that "[T]he various types of cancers have different causative agents, involve different cellular mechanisms, and consequently differ in treatment protocol." The Examiner quotes Golub *et al.* stating that "cancer classification has been based primarily on morphological appearance of the tumor, and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy."

However, the Golub article, cited by the Examiner to illustrate unpredictability, discloses a means whereby predictability is obtainable by classifying tumors according to gene expression. Golub *et al.* teaches (page 531, left column) that "[I]mprovements in cancer classification have been central to advances in cancer treatment."

Golub observes that classification of cancers by measures such as morphological appearance lack the desired level of predictability of clinical outcomes or therapy responses. But, Golub states that monitoring tumor gene expression can provide predictability, and that "class discovery methods could also be used to search for fundamental mechanisms that cut across distinct types of cancers" (Golub *et al.*, page 535, center column). Golub *et al.* teaches that though cancers vary broadly, they may be classified by genetic expression of proteins, *e.g.*, topoisomerase II (Golub *et al.*, page 533, left column), and that such classification may provide useful diagnostic and therapeutic utility.

Claim 40, as herein amended, recites treatment of a subset of cancers that are characterized, as taught by Golub *et al.*, not by morphology, or by cellular origin, but rather by genetic expression, *i.e.*, expression, by the tumor, of a cyclooxygenase that promotes the production of prostaglandins.

Unpredictability in the pharmaceutical arts is mitigated in the present case, because the claim in issue is directed to treating a tumor that expresses a cyclooxygenase, by administering an agent selected from a genus of compounds shown experimentally in

the specification to inhibit COX-2. The state of the art, at the time of the application, recognized that tumors expressing a cyclooxygenase would respond to COX-2 inhibitors. The state of the art (Golub *et al.*) further recognized monitoring tumor gene expression as a means to provide predictability, and thereby provide a tool to “target specific therapies to pathogenetically distinct tumor types” Golub *et al.*, (page 531, left column).

The Examiner cites, at page 4, line 7 of the Action, *In re Fisher* (166 USPQ 18) as holding that more specific enablement is required in more unpredictable areas. In *In re Fisher*, the Board was examining a claim that recited an open ended range as follows.

“substantially all “preparations” produced synthetically or by breakdown of the 39 amino acid polypeptides in any manner to form a polypeptide product of lesser molecular weight containing any number (claim 5) or at least 24 (claim 4) of the amino acids as long as the product exhibits, without the stated side effects, activity equal to at least 1 International Unit of ACTH per milligram. (emphasis added) *Id* at 23.

The Board in *Fisher* noted that the specification disclosed potencies from 1.11 to 2.3 International Units. The Board’s ruling was based on the inadequacy of disclosure of a numerical range. The disclosed numerical range 1.1 - 2.3 was deemed by the Board to be insufficient to support the claim to a numerical range from 1 to “no upper limit.”

The presently rejected claims do not recite a numerical range lacking an upper limit as was the issue in *Fisher*. Claims 34-36 recite a method for treating a cyclooxygenase-mediated disorder by administering “an effective amount of a compound according to formula I.” The specification provides support for the cyclooxygenase inhibitory activity of compounds of formula I. The specification discloses and incorporates by reference the teaching of US patent 5,972,986 that neoplasias that express a cyclooxygenase may be treated by administering a cyclooxygenase inhibitor.

The Examiner states at page 5, line 11-13 that, “[O]ne of skill in the art would need to determine what diseases would be benefited (treated) by inhibition of cyclooxygenase. . .” Contrariwise, the practice of the invention does not require that one determine what diseases could be treated. Applicant’s patent specification points out numerous cyclooxygenase-mediated disorders including inflammatory disorders such as rheumatoid arthritis and other disorders listed at column 12, line 1-25, cyclooxygenase

expressing neoplasias such as those listed at column 12, line 45-55, and angiogenesis-mediated disorders such as those listed from column 12, line 66 to column 13, line 4.

D. Analysis of *Wands* factors in *In re Wands*

Analysis of the *Wands* factors, as the factors were weighed by the court in *In re Wands*, shows that the claims presently at issue are enabled under 35 U.S.C. § 112, first paragraph. In *In re Wands*, the court found those claims were enabled, and stated:

Wands' disclosure provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known.

The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody. *In re Wands*, 8 USPQ2d at 1406 (emphasis added).

In the present application, the claims at issue recite a method of treating a cyclooxygenase-mediated disorder (claims 34-36), and a tumor that expresses cyclooxygenase (claim 40), comprising administering a compound that is a member of a defined chemical genus shown experimentally to inhibit COX-2.

The specification provides:

- a defined genus of compounds that selectively inhibit COX-2;
- a working example providing an experimental protocol capable of determining whether a compound inhibits COX-2; and
- a working example providing an experimental protocol for determining whether a compound inhibits tumor cell growth.

Knowledge in the art included:

- knowledge and skill sufficient for determining which tumors express a cyclooxygenase by experimentation that was routine in the art; and
- knowledge that tumors expressing a cyclooxygenase are treatable with cyclooxygenase inhibitors.

Where the art typically engages in a complex, but routine degree of experimentation, such activity, as a step in practicing the invention, is not undue


experimentation proscribed by 35 U.S.C. § 112, first paragraph, under the reasoning employed by the court in *In re Wands*.

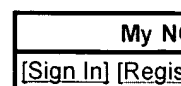
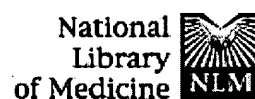
**Conclusion**

Based on the foregoing, all claims are believed in condition for allowance. An early and favorable action toward that end is earnestly solicited.

Respectfully submitted,

E. PREMKUMAR REDDY, et al.

By   
DANIEL A. MONACO  
Registration No. 30,480  
DRINKER BIDDLE & REATH LLP  
One Logan Square  
18<sup>th</sup> and Cherry Streets  
Philadelphia, PA 19103-6996  
(215) 988-3312 - Phone  
(215) 988-2757 - Fax  
Attorney for the Applicant



All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Book

Search PubMed for Go Clear

Limits Preview/Index History Clipboard Details

Display Abstract Show 20 Sort by Send to

All: 1 Review: 0

About Entrez

Text Version

Entrez PubMed

Overview

Help | FAQ

Tutorial

New/Noteworthy

E-Utilities

PubMed Services

Journals Database

MeSH Database

Single Citation Matcher

Batch Citation Matcher

Clinical Queries

Special Queries

LinkOut

My NCBI (Cubby)

Related Resources

Order Documents

NLM Catalog

NLM Gateway

TOXNET

Consumer Health

Clinical Alerts

ClinicalTrials.gov

PubMed Central

1: Carcinogenesis. 2000 Feb;21(2):139-46.

Related Articles, Links

FREE full text article at  
carcin.oupjournals.org**Cyclooxygenase-2 expression in human pancreatic adenocarcinomas.****Yip-Schneider MT, Barnard DS, Billings SD, Cheng L, Heilman DK, Lin A, Marshall SJ, Crowell PL, Marshall MS, Sweeney CJ.**

Department of Medicine, Department of Biochemistry and Walther Oncology Center, Indiana University School of Medicine, Indianapolis 46202, USA. myipschn@iupui.edu

Cyclooxygenase-2 (COX-2) expression is up-regulated in several types of human cancers and has also been directly linked to carcinogenesis. To investigate the role of COX-2 in pancreatic cancer, we evaluated COX-2 protein expression in primary human pancreatic adenocarcinomas (n = 23) and matched normal adjacent tissue (n = 11) by immunoblot analysis. COX-2 expression was found to be significantly elevated in the pancreatic tumor specimens compared with normal pancreatic tissue. To examine whether the elevated levels of COX-2 protein observed in pancreatic tumors correlated with the presence of oncogenic K-ras, we determined the K-ras mutation status in a subset of the tumors and corresponding normal tissues. The presence of oncogenic K-ras did not correlate with the level of COX-2 protein expressed in the pancreatic adenocarcinomas analyzed. These observations were also confirmed in a panel of human pancreatic tumor cell lines. Furthermore, in the pancreatic tumor cell line expressing the highest level of COX-2 (BxPC-3), COX-2 expression was demonstrated to be independent of Erk1/2 activation. The lack of correlation between COX-2 and oncogenic K-ras expression suggests that Ras activation may not be sufficient to induce COX-2 expression in pancreatic tumor cells and that the aberrant activation of signaling pathways other than Ras may be required for up-regulating COX-2 expression. We also report that the COX inhibitors sulindac, indomethacin and NS-398 inhibit cell growth in both COX-2-positive (BxPC-3) and COX-2-negative (PaCa-2) pancreatic tumor cell lines. However, suppression of cell growth by indomethacin and NS-398 was significantly greater in the BxPC-3 cell line compared with the PaCa-2 cell line (P = 0.004 and P < 0.001, respectively). In addition, the three COX

inhibitors reduce prostaglandin E(2) levels in the BxPC-3 cell line. Taken together, our data suggest that COX-2 may play an important role in pancreatic tumorigenesis and therefore be a promising chemotherapeutic target for the treatment of pancreatic cancer.

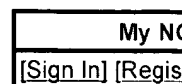
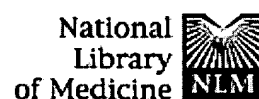
PMID: 10657949 [PubMed - indexed for MEDLINE]

---

Display  ☐ Show  ☐ Sort by  ☐ Send to  ☐

[Write to the Help Desk](#)  
[NCBI](#) | [NLM](#) | [NIH](#)  
[Department of Health & Human Services](#)  
[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Jun 27 2005 04:57:20



All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for   

Limits Preview/Index History Clipboard Details

Display Abstract Show 20 Sort by Send to

About Entrez

Text Version

All: 1 Review: 0

Entrez PubMed

Overview

Help | FAQ

Tutorial

New/Noteworthy

E-Utilities

PubMed Services

Journals Database

MeSH Database

Single Citation Matcher

Batch Citation Matcher

Clinical Queries

Special Queries

LinkOut

My NCBI (Cubby)

Related Resources

Order Documents

NLM Catalog

NLM Gateway

TOXNET

Consumer Health

Clinical Alerts

ClinicalTrials.gov

PubMed Central

☐ 1: Jpn J Cancer Res. 1999 Dec;90(12):1338-43.

Related Articles, Links

**Cyclooxygenase-2 (COX-2) mRNA expression levels in normal lung tissues and non-small cell lung cancers.****Ochiai M, Oguri T, Isobe T, Ishioka S, Yamakido M.**

Second Department of Internal Medicine, Hiroshima University Faculty of Medicine, Kasumi.

One of the cyclooxygenase (COX) isoforms, COX-2, is overexpressed in various human cancers. In this study, we examined the gene expression levels of COX-2 in primary non-small cell lung cancers (NSCLC), metastatic lymph nodes, and normal lung tissues. The expression levels of the COX-2 gene were assessed by means of the reverse transcription polymerase chain reaction in 76 autopsy samples (29 primary NSCLC, 29 corresponding normal lung tissues, and 9 metastatic lymph nodes). The expression levels in NSCLC (both adenocarcinomas and squamous cell carcinomas) were significantly higher than in normal lung tissues and were significantly higher in adenocarcinomas than in squamous cell carcinomas. Differences between the levels of expression of COX-2 in primary tumors and their corresponding metastatic lymph nodes in 9 adenocarcinoma patients were not significant. Our results indicate that COX-2 may be associated with carcinogenesis of NSCLC, and that it may be a target for the treatment of NSCLC.

PMID: 10665651 [PubMed - indexed for MEDLINE]

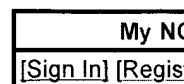
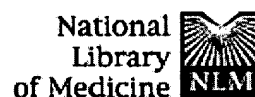
Display Abstract Show 20 Sort by Send to

[Write to the Help Desk](#)[NCBI](#) | [NLM](#) | [NIH](#)

Department of Health &amp; Human Services

[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Jun 27 2005 04:57:20



All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for   

Limits Preview/Index History Clipboard Details

Display Abstract Show 20 Sort by Send to

All: 1 Review: 0 

About Entrez

Text Version

Entrez PubMed

Overview

Help | FAQ

Tutorial

New/Noteworthy

E-Utilities

PubMed Services

Journals Database

MeSH Database

Single Citation Matcher

Batch Citation Matcher

Clinical Queries

Special Queries

LinkOut

My NCBI (Cubby)

Related Resources

Order Documents

NLM Catalog

NLM Gateway

TOXNET

Consumer Health

Clinical Alerts

ClinicalTrials.gov

PubMed Central

☐ 1: Am J Pathol. 2000 Jul;157(1):29-35.

Related Articles, Links

**Enhanced expression of cyclooxygenase-2 in high grade human transitional cell bladder carcinomas.****Komhoff M, Guan Y, Shappell HW, Davis L, Jack G, Shyr Y, Koch MO, Shappell SB, Breyer MD.**

Division of Nephrology, Department of Medicine, Vanderbilt University, Nashville, TN, USA.

Studies in human and animal models have shown that cyclooxygenase (COX)-2 is up-regulated in several epithelial carcinomas including colon, breast, and lung. To elucidate the possible involvement of COX-2 in human bladder cancer we examined the expression of COX isoforms in benign tissue and in bladder carcinoma specimens. Paraffin embedded tissues from 75 patients with urothelial carcinomas were immunostained with specific antibodies raised against COX-1 and COX-2. COX-1 expression was detected in smooth muscle cells in both benign and malignant bladders. COX-2 immunoreactivity was absent in benign tissue and in specimens with low-grade urothelial carcinoma (0/23). In contrast, expression of COX-2 was detected in malignant epithelial cells in 38% (17/47) of specimens with high-grade urothelial carcinomas. Expression of COX-2 in high-grade bladder cancer was confirmed by radioactive in situ hybridization using a COX-2-selective riboprobe. Both immunohistochemistry and in situ hybridization showed COX-2 expression in a small subset of malignant cells. COX-2 mRNA was also expressed in three out of seven malignant urothelial cell lines. These data demonstrate elevated expression of COX-2 in a high percentage of high-grade bladder carcinomas, suggesting a possible role of COX-2 in the progression of bladder urothelial carcinoma and supporting its potential as a therapeutic target in human bladder carcinoma.

PMID: 10880372 [PubMed - indexed for MEDLINE]

Display  Show  Sort by  Send to

[Write to the Help Desk](#)

[NCBI](#) | [NLM](#) | [NIH](#)

[Department of Health & Human Services](#)

[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Jun 27 2005 04:57:20